

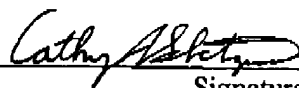
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**CERTIFICATION OF FACSIMILE TRANSMISSION  
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Attorney Docket No. 9233.71

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re: Soltero et al.

Application Serial No.: 10/036,744

Filed: December 21, 2001

For: *Methods of synthesizing insulin polypeptide-oligomer conjugates, and proinsulin polypeptide-oligomer conjugates and methods of synthesizing same*

Confirmation No.: 3700

Group Art Unit: 1646

Examiner: R. Teller

Submittal of:

**Response (3 pages)**

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Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450**RESPONSE**

This is responsive to the Office Action mailed January 16, 2004 regarding the above-referenced patent application.

Claims 1-53, 248-281, 371-398 and 446-458 are pending herein.

**I. Claim Rejections under 35 USC § 102(b)**

The Office Action states that claims 1-53, 248-281, 371-398 and 446-458 are rejected under 35 USC § 102(b) as allegedly being anticipated by Ekwuribe (US Patent No. 6,309,633). Applicants respectfully traverse this rejection.

"For a claim to be invalid on the basis of anticipation under section 102(b), 'the invention must have been known to the art in the detail of the claim; that is, all of the elements and limitations of the claim must be shown in a single prior art reference, arranged as in the claim.'"<sup>1</sup> Anticipation requires that the identical invention that is claimed was previously known to others and thus is not new.<sup>2</sup>

The examiner has not shown that "all of the elements and limitations of the claim" are provided in Ekwuribe. In particular, Ekwuribe does not teach coupling an oligomer with a proinsulin polypeptide in a manner, which results in *coupling of the oligomer to the insulin polypeptide portion thereof*. Further, Ekwuribe does not describe that one or more peptides are *cleaved from the conjugate* to provide the insulin polypeptide-oligomer conjugate. In other words, Ekwuribe does not teach the *conjugate-then-cleave* approach claimed in the present invention. It is well recognized in the art that conjugation is

<sup>1</sup> Halliburton Energy Svcs., Inc. v. Weatherford Int'l. Inc., 2003 U.S. Dist. LEXIS 15130 (U.S. Dist. , 2003) (citing Karsten Mfg. Corp. v. Cleveland Golf Co., 242 F.3d 1376, 1383 (Fed. Cir. 2001)).

<sup>2</sup> Continental Can Co. USA, Inc., v. Monsanto Co., 948 F.2d 1264, 1267 (Fed. Cir. 1991) (citations omitted).

Attorney Docket No. 9233.71  
Application Serial No.: 10/036,744  
Page 2 of 3

typically used as a means for inhibiting enzymatic and chemical cleavage of therapeutic peptides. The claimed invention is a result of the surprising discovery of an advantageous method of synthesizing a conjugated insulin polypeptide-oligomer conjugate, using a *conjugate-then-cleave* approach. This approach goes against the traditional view, and the approach taught by Ekwuribe, that the purpose of conjugation is to *inhibit* cleavage.

Thus, applicants respectfully submit that the present invention is not anticipated by Ekwuribe and request that this rejection be withdrawn.

## II. Claim Rejections under 35 USC 103

The Office Action states that claims 1-53, 248-281, 371-398 and 446-458 are rejected under 35 USC § 103 as allegedly being unpatentable over Ekwuribe (US Patent No. 6,309,633). Applicants respectfully traverse this rejection.

It is well established in the case law that to establish a *prima facie* case of obviousness, three basic criteria must be met. First, the prior art reference must teach or suggest all the claim limitations. Second, there must be some suggestion or motivation, either in the reference itself or in the knowledge generally available to one of ordinary skill in the art, to modify the reference to produce the claimed invention with all its limitations. Third, the prior art teachings must provide a reasonable expectation of success in carrying out the claimed invention. The teaching or suggestion, and thus the motivation to modify the art teachings to produce the claimed invention and the reasonable expectation of success must both be found in the prior art, not in Applicant's disclosure.<sup>3</sup> Applicants respectfully submit that these criteria have not been met.

Ekwuribe does not teach or suggest all the claim recitations of the present invention, as set forth in the arguments presented above in opposition to the rejection under 35 USC § 102(b), which are incorporated herein. Specifically, Ekwuribe does not teach or suggest the novel and unexpected *conjugate-then-cleave* approach claimed by the applicants. In fact, Ekwuribe teaches away from the *conjugate-then-cleave* approach by emphasizing that the conjugation approaches described therein function to *inhibit cleavage* of peptides.<sup>4</sup> As stated by the Court of Appeals for the Federal Circuit, "...a reference will teach away if it *suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought.*"<sup>5</sup> The line of development flowing from Ekwuribe is towards the use of conjugation to inhibit cleavage. Thus, one of ordinary skill in the art

<sup>3</sup> See MPEP § 2143.

<sup>4</sup> See Ekwuribe et al., column 1, lines 17-33.

<sup>5</sup> In re Gurley, 27 F.3d 551, 553 (Fed. Cir. 1994).


Attorney Docket No. 9233.71  
Application Serial No.: 10/036,744  
Page 3 of 3

would not be motivated to modify Ekwuribe to use applicants' approach of conjugation prior to cleavage and in fact would be motivation by the teachings of Ekwuribe to avoid conjugation prior to cleavage. Because Ekwuribe provides no motivation to produce the claimed invention, this reference also provides no reasonable expectation of success. For the foregoing reasons, applicants respectfully submit that the present invention is not obvious in view of the teachings of Ekwuribe and request that this rejection be withdrawn.

Applicants respectfully submit that claims 1-53, 248-281, 371-398 and 446-458 are in form for allowance and request that a Notice of Allowance be issued. The Examiner is encouraged to contact the undersigned directly if such contact will expedite the examination and allowance of the pending claims.

No fee is believed due with this response. However, the Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-0220.

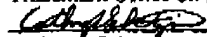
Respectfully submitted,

  
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